REMARKS

Introductory Comments:

Claims 2, 5, 6 and 9-22 were examined in the Office Action under reply and stand variously rejected under 35 U.S.C. §112, first and second paragraphs. These rejections are respectfully traversed as discussed more fully below.

Overview of the Above Amendments:

Claims 5, 9-13, 17 and 18 have been amended to recite the invention with greater particularity. Specifically, the recitation of "90% sequence identity" has been eliminated from claims 5 and 12, and replaced with a recitation of "95% sequence identity" in claims 10 and 13. Support for this amendment can be found at, e.g., page 14, line 23 of the specification. Additionally, the references to figures have been replaced in claims 5, 9-13 and 18 with the corresponding sequence identifiers. Claims 9 and 13 have also been amended to recite that the sequences are in 5' to 3' order. Support for this recitation can be found throughout the application at, e.g., Figure 1A. Claim 10 has been rewritten in independent format. Finally, claim 17 has been amended to spell out the abbreviations as requested by the Office.

Amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications containing the unamended claims.

Claim Objections:

Claim 17 was objected to based on the use of abbreviations. The Office requested the abbreviations be spelled out. Applicants submit that the recited promoters are well known and commonly referred to by the names presented in claim 17. Nevertheless, the full spelling for all of the promoters in claim 17, with the exception of the SRα promoter, has been inserted. Including a description of the well-known SRα promoter in the claim would be cumbersome. As explained in Theron et al., *J. Biotechnol.* (2000) 77:179-189 (abstract), appended for the Examiner's convenience, the SRα promoter is an association of the SV40 early gene promoter

with the R region plus the first 39 nucleotides of the U5 region from HTLV-1. Accordingly, the term "SRα promoter" in the claim is believed to be clear.

Claim 13 was objected to as being a substantial duplicate of claim 5. Claims 5 and 13 have both been amended. Claim 5 no longer includes a recitation of percent identity whereas claim 13 does. Thus, these claims are not substantial duplicates of each other and this basis for objection should be withdrawn.

Claims 2, 5, 6 and 9-22 were objected to as referring to a figure rather than a sequence identifier. The claims have been amended to refer to sequence identifiers in place of figures. Thus, this basis for objection has been overcome.

Rejection Under 35 U.S.C. §112, Second Paragraph:

Claims 2, 5, 6 and 9-22 were rejected under 35 U.S.C. §112, second paragraph as indefinite. The Office finds the terms "inclusive" and "depicted in" unclear. These terms have been eliminated from the claims. Thus, these bases for rejection have been overcome and withdrawal thereof is respectfully requested.

Rejection Under 35 U.S.C. §112, First Paragraph:

Claims 2, 5, 6, 9, 10 and 12-22 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office argues:

> Applicants claim a genus of hCMV Intron A fragments comprising sequences having at least 90% sequence identity to contiguous sequences found at positions 1-25 or 1-51 and 775-820 or 741-820.
>
> * * *
>
> The instant specification describes the generation of thirteen CMV Intron A fragments by sequentially greater internal deletions leaving the 5' and 3' nucleotide sequences intact which include part or all of nucleotides 1-25 or 1-51 and 775-820 or 741-820 (figure 3). Eleven of the fragments are able to direct transcription of luciferase to levels greater than full length intron A and one fragment to levels greater than 2-fold over full length intron A (see figure 4). A deletion mutant pCON3 Intron A is taught...in which ten of the nucleotides between 741 and 820 are substituted. However, the disclosure does not teach any fragments having at least 90% sequence identity to contiguous sequences found at positions 1-25 or 1-51 and 775-820 of SEQ ID 1 that direct expression of coding sequences. There is no actual reduction to practice or clear depiction of what structures or properties are required for generation of an Intron A fragment with

90% identity to the sequences found at positions 1-25 or 1-51 and 775-820 or 741-820 of SEQ ID 1.

Office Action, pages 4-5. However, applicants disagree.

First, several of the claims subject to the present rejection do not include a recitation of 90% sequence identity. Specifically, this limitation does not occur in rejected claims 9, 15, 16, 18 and 20-22. Moreover, the recitation of percent identity has been eliminated from claims 5, 12, 14, 17 and 19. Accordingly, the only claims that currently recite a percent identity are claims 10 and 13. Thus, this basis for rejection does not apply to claims 2, 5, 6, 9, 11, 12 and 14-22 and should be withdrawn.

With respect to claims 10 and 13, both of these claims have been amended to replace the recitation of "90%" sequence identity with "95%" sequence identity. Moreover, the 95% sequence identity is with respect to designated nucleotide sequences of SEQ ID NO:1 and SEQ ID NO:3. Additionally, claims 10 and 13 both require when the fragment is present in an expression construct, the expression construct "directs the transcription of a coding sequence present in the construct at levels equal to, or greater than, those levels achieved by an expression construct that includes a corresponding intact, full-length Intron A sequence."

Applicants again direct the Examiner's attention to the Patent Office's own guidelines regarding the written description requirement. Example 14 of the Patent Office's "Synopsis of Application of Written Description Guidelines" is clear that a **single** disclosed species may be representative of a "product-by-function" genus when all members exhibit structural identity to a reference compound (here, SEQ ID NOS:1 and 3) and when an assay is provided for identifying all variants having the claimed activity (such as detailed in Example 2). The Examiner has failed to point out any substantive distinctions between Example 14 and the recitations in the present claims in the Office Action. In fact, Example 14 of the Synopsis is completely on point. Example 14 is reproduced below:

Claim:

A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B.

Analysis:

... The procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art. ....

There is actual reduction to practice of a single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO:3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO:3. The **single species disclosed** is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 U.S.C. § 112, first paragraph as providing adequate written description for the claimed invention. (Example 14, emphasis added.)

Like Example 14, applicants in the pending case have provided a limit to the structural identity (now 95% identity), a specified activity of the variants (directs the transcription of a coding sequence present in the construct at levels equal to, or greater than, those levels achieved by an expression construct that includes a corresponding intact, full-length Intron A sequence) and methods for identifying constructs exhibiting the specified activity (See, e.g., Example 2 of the application). Therefore, as in PTO Example 14, the multiple species disclosed in the application are representative of the genus as a whole.

Accordingly, one of skill in the art would conclude applicant was in possession of the necessary common attributes possessed by the members of the genus, and it is clear that, as concluded in PTO Example 14, the present application provides adequate written description for the substance of claims 10 and 13. Withdrawal of the rejection under 35 U.S.C. §121, first paragraph is therefore respectfully requested.

CONCLUSION

Applicants respectfully submit that the claims define a patentable invention. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further written communications in this application to:

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The stimulation of gene expression by the R region from HTLV-1 and BLV.

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The 5' untranslated regions (5'UTR) of mRNA are known to stimulate or inhibit more or less translation. SR alpha, an association of SV40 early gene promoter and of the R region plus the first 39 nucleotides of the U5 region (designated as R) from the human T-cell leukemia virus (HTLV-1) is currently used to stimulate expression of various coding regions. Its effect is considered to take place at the translational level. In all studies published so far, the R region was associated with the promoter and 5'UTR from SV40 early genes. In the present work, the role of SV40 5'UTR and HTLV-1R region was evaluated separately using different promoters, reporter genes and cells. Both SV40 5'UTR (SU) and R region (R) from HTLV-1 stimulated separately the expression of adjacent reporter genes. When associated, the SV40 5'UTR and the R region from HTLV-1 (SUR) were a more potent stimulator of gene expression and their effects were more than additive. This effect was very potent in HeLa and HC11 cells and almost inexistent in CHO and COS 7 cells. It was of various intensity in other cell types including bird and fish cells. The presence of SUR in gene constructs favoured the accumulation of the mRNAs. SUR stimulated gene expression when added between the cap and the initiation codon. Unexpectedly, SUR was never inhibitory. SUR can therefore be considered essentially as potent and specific stimulator of gene expression favoring mRNA accumulation.